Reaction of Trifluoromethyl Ketones. VI.[1] Synthesis of Trifluorinated Analogues of Monoterpenes[2]

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The ene reaction product of trifluoroacetone with cyclohexene, 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-cyclohexene (1), was converted to trifluorinated analogues of *p*- and *m*-menthane derivatives. For introduction of a functional group at suitable positions of the cyclohexene ring, oxidation of 1 was carried out to give 1-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-ol (2), 4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (3) and 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (4). Selenium dioxide gave only a small amount of 2. The best oxidizing reagent among those examined was *tert*-butyl hydroperoxide with chromium trioxide or chromium hexacarbonyl as a catalyst. In the presence of basic compounds such as pyridine or dimethylpyrazole, chromium trioxide gave a larger amount of 4 than 3, while in the presence of acetic acid, 3 was formed preferentially though the total yield was very low. Oxidation of 1 with *tert*-butyl hydroperoxide catalyzed by chromium hexacarbonyl gave 3 in excess over 4 in satisfactory yields. Treatment of the carbonyl compounds (3 or 4) with methylmagnesium iodide gave a *p*- or *m*-menthane skeleton with fluorine substituents, and these products were converted to some fluorine analogues of monoterpenes.

Keywords trifluoromethyl; menthane; oxidation; homoallyl alcohol; fluorine; methylmagnesium iodide; reduction; dehydration; ene-reaction product

The ene reaction of trifluoromethyl ketones has been investigated, and this reaction was found to be very useful for the synthesis of trifluoromethylated homoallyl alcohols.[3-5] We are now engaged in the derivatization of these homoallyl alcohols to various kinds of trifluoromethylated compounds. In the previous papers, we reported the cyclization of the homoallyl alcohols to 2-(trifluoromethyl)tetrahydrofurans[6] and dehydration of the homoallyl alcohols to trifluoromethylated dienes.[1] This paper is concerned with the allylic oxidation of the ene reaction product of trifluoroacetone with cyclohexene and the derivatization of the ketone compounds to trifluorinated analogues of menthane derivatives. Menthane derivatives are useful intermediates for the synthesis of many kinds of monoterpenes and sesquiterpenes, as shown in Chart 1. Therefore, synthesis of fluorine analogues of menthanes should provide starting materials for fluorine analogues of many kinds of natural products.

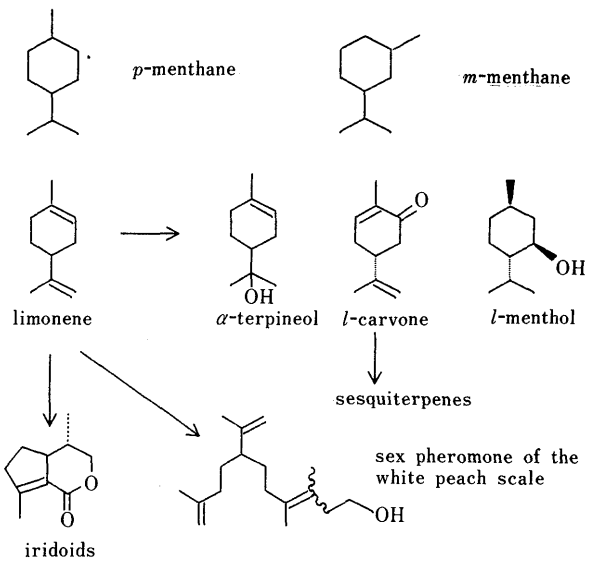


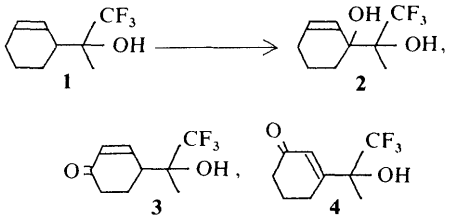
Chart 1

The ene reaction product of trifluoroacetone with cyclohexene, 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (**1**), seemed to be a good precursor for menthane derivatives. For the derivatization of menthanes from **1**, introduction of a functional group at the 3- or 4-position is necessary. First, bromination of **1** with *N*-bromosuccinimide was examined, but the starting material was recovered in spite of various attempts. Next, allylic oxidation of **1** with selenium dioxide was attempted. In this case, only a small amount of 1-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-ol (**2**) was obtained with recovery of most of the starting material. The structure of **2** was determined from the nuclear magnetic resonance (NMR) spectrum, which showed signals due to two hydroxylic and two olefinic hydrogens, but no alpha hydrogen to a hydroxyl group. Since the yield was low and the product was not of current interest to us, we did not determine its stereochemistry, but it is interesting that this reaction gave only one diastereomer. Lead tetraacetate did not give any isolable products.

Oxidation of **1** with chromium trioxide–pyridine gave 4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**3**) and 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**4**) in yields of 5% and 11%, respectively, with recovery of 33% of the starting material. The NMR spectrum of **3** showed two olefinic hydrogens and one hydrogen alpha to the 2,2,2-trifluoro-1-hydroxy-1-methylethyl group, while that of **4** showed one olefinic hydrogen. No diastereomer of **3** was detected. This fact shows that isomerization did not occur during the formation of **3**.

Next, the oxidation of **1** with 3,5-dimethylpyrazole (DMP) chromium trioxide complex, which was reported to be a good reagent for allylic oxidation,[7] gave a mixture of **3** and **4** (ratio, 1 : 4) in 51% yield. These results suggested that a base promoted the oxidation at the 1-position rather than at the 4-position. Namely, the strong electron-withdrawing effect of the trifluoromethyl group increases the acidity of the proton at the 1-position, and migration of the double

TABLE I. Oxidation of Compound **1**



Reagent	Conditions	Products
NBS/AIBN	Reflux in C_6H_6	No reaction
SeO_2	Reflux in EtOH 24 h	**2** (21%)
CrO_3/pyridine	r.t. in CH_2Cl_2 17 h	**3**+**4** (1:2, 16%)
CrO_3/DMP	−20 °C in CH_2Cl_2	**3**+**4** (1:4, 51%)
CrO_3/AcOH	r.t. 15 h	**3**+**4** (2:1, <20%)
tert-BuOOH/CrO_3	r.t. 14 h	**3**+**4** (2:1, 67%)
tert-BuOOH/$Cr(CO)_6$	Reflux in CH_3CN	**3**+**4** (2:1, 55%)

r.t., room temperature.

bond and introduction of an oxygen function at the 3-position occur. To obtain an oxidation product at the 4-position preferentially, oxidation in non-basic media was examined. Thus, **1** was treated with chromium trioxide in acetic acid or acetic acid–water. This reaction gave a mixture of **3** and **4** in a ratio of 2:1 as expected, but the total yield was low. Oxidation of **1** with *tert*-butyl hydroperoxide in the presence of a catalytic amount of chromium trioxide[8] gave a much higher yield of a mixture of **3** and **4**, though this reaction required a large excess (about 10 eq) of *tert*-butyl hydroperoxide. Use of chromium hexacarbonyl as a catalyst[9] allowed the amount of *tert*-butyl hydroperoxide to be decreased to 1.5 mol and still gave 55% yield of the mixture of **3** and **4**. The ratio of **3** and **4** was not affected by the change of reaction conditions mentioned above. Separation of **3** and **4** could be effected by medium-pressure liquid chromatography. Therefore, we had in hand the carbonyl compounds which could be converted to fluorine analogues of menthane derivatives by the introduction of a methyl group (see Table I).

First, **3** was treated with methylmagnesium iodide to give two isomers of 1-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-ol (1*R**, 4*S**: **5a** and 1*R**, 4*R**: **5b**). The structure of **5b** was determined by X-ray analysis.[10] This unambiguously determined the stereochemistry of the ene reaction and the structure of the oxidation product.

Next, trifluoro analogues of α-terpineol and limonene were derivatized from **3**. Hydrogenation of **3** in the presence of Pd–C gave 4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-cyclohexanone (**6**) in a quantitative yield. Treatment of **6** with methylmagnesium iodide gave 1-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexanol (**7**) as a mixture of two diastereomers (ratio 2:3), which were separated by column chromatography. The latter eluate (major product) was tentatively assigned the *cis* relationship of the 1-methyl group and 4-substituent by comparison of the order of elution in column chromatography with that of **5**. Dehydration of **7** with phosphoryl chloride and pyridine at room temperature gave 1-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (trifluoro-α-terpineol, **8**) in 67% yield. This was a mixture of two

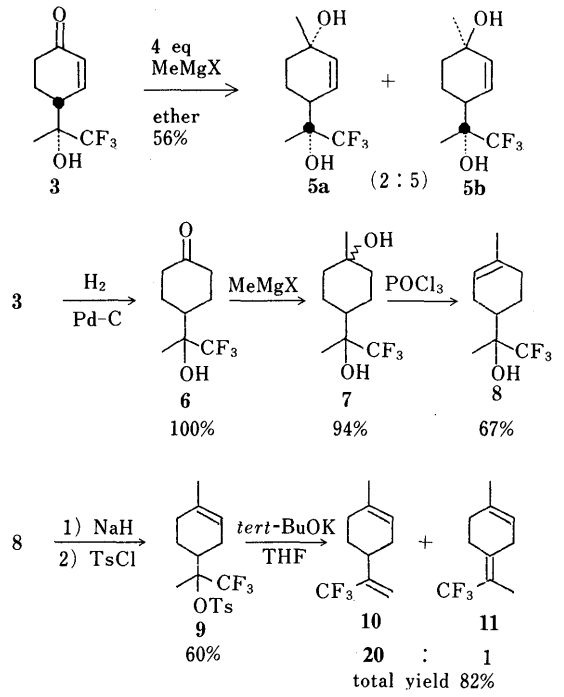
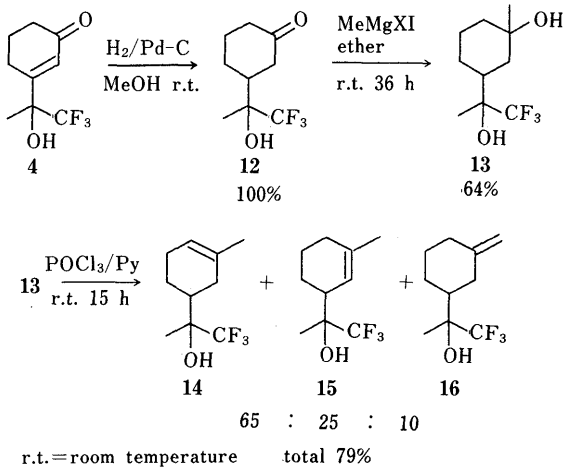


Chart 2



r.t.=room temperature total 79%

Chart 3

diastereomers (1:1). Tosylation of **8** gave a tosyl ester **9**, which was treated with *tert*-BuOK to give 1-methyl-4-[1-(trifluoromethyl)ethenyl]cyclohexene (trifluorolimonene, **10**) with a small amount of 1-methyl-4-[methyl(trifluoromethyl)methylene]cyclohexene (**11**) (ratio of **10**:**11**=20:1, total yield 82%). Thus, a bulky base abstracted a methyl proton to give an *exo*-methylene compound preferentially. These syntheses of trifluoro analogues of *p*-menthane derivatives are summarized in Chart 2.

Finally, the synthesis of trifluoro analogues of *m*-menthane derivatives is presented. Hydrogenation of 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**4**) gave 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-cyclohexanone (**12**, 1:1 mixture of diastereomers) in a quantitative yield. Treatment of **12** with methylmagnesium iodide gave 1-methyl-3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexanol (**13**) in 64% yield with recovery of 36% of the starting material. This compound was a mixture of four diastereomers (4:4:1:2). Dehydration of **13**

with phosphoryl chloride and pyridine gave 2-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (**14**), 1-methyl-3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (**15**) and 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-1-methylenecyclohexane (**16**) in a ratio of 65:25:10. Compounds **14** and **15** are trifluoro analogues of the so-called sylveterpineol (see Chart 3).

In conclusion, the ene reaction product **1** was converted through rather simple procedures into trifluoro analogues of menthane derivatives, which are difficult to synthesize *via* other routes. These results show the usefulness of our ene reaction of trifluoromethyl ketones.

Experimental

The starting material, 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (**1**), was synthesized according to the literature.[4] ^{1}H-NMR spectra were obtained on JNM-FX90Q and JNM-GX400 spectrometers. ^{19}F-NMR spectra were recorded on the JNM-FX90Q spectrometer, using benzotrifluoride as an internal standard (upper field taken as plus). Preparative gas-liquid chromatography (GLC) was performed on a Hitachi-163 apparatus; column, 15% SE-30 (L = 1 m, i.d. = 4 mm); carrier He, 30 ml/min, unless otherwise stated.

Attempted Bromination of 3-(2,2,2-Trifluoro-1-hydroxy-1-methylethyl)-cyclohexene (1) with *N*-Bromosuccinimide A solution of **1** (194 mg, 1 mmol) and *N*-bromosuccinimide (NBS) (178 mg, 1 mmol) in CCl_4 (5 ml) was refluxed in the presence of azobisisobutyronitrile (AIBN) (1 mg) for 18 h. The reaction mixture was analyzed by GLC (column, 15% SE-30 1 m × 4 mm; temperature, 140 °C; carrier gas, N_2 (40 ml/min)), but only the starting material was observed.

Oxidation of 1 with $Pb(OAc)_4$ A solution of **1** (97 mg, 0.5 mmol) and $Pb(OAc)_4$ (443 mg, 1 mmol) in AcOH (1 ml) was heated at 100 °C for 12 h. The reaction mixture was analyzed by thin-layer chromatography (TLC) (SiO_2, CH_2Cl_2); it contained many inseparable products.

Allylic Oxidation of 1 with SeO_2 A solution of **1** (194 mg, 1 mmol) and SeO_2 (111 mg, 1 mmol) in EtOH (2 ml) was refluxed for 24 h under stirring. The reaction mixture was filtered through a Celite layer, and the filtrate was extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and NaCl, dried over $MgSO_4$ and concentrated under vacuum. The residue was analyzed by GLC (15% SE-30, 1 m × 4 mm, 90 °C, N_2, 40 ml/min); it contained a product, 1-(2,2,2,-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-ol (**2**, 21%), and unchanged **1** (61%, GLC peak area). Compound **2** was separated by preparative GLC (15% SE-30, 1 m × 4 mm 80 °C, He, 30 ml/min). **2**: Colorless oil, mass spectrum (MS) *m/z*: 210 (M^+). HRMS Calcd for $C_9H_{13}F_3O_2$: 210.087. Found: 210.086. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, s), 1.68—1.82 (3H, m), 1.90—2.03 (2H, m), 2.05—2.15 (1H, m), 2.08 (1H, s), 3.66 (1H, s), 5.85 (1H, br d, J = 10.1 Hz), 6.04 (1H, ddd, J = 10.1, 4.6, 2.1 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 11.92 (s).

Oxidation of 1 with CrO_3–Pyridine Complex A solution of **1** (194 mg, 1 mmol) in CH_2Cl_2 (1 ml) was added to a solution of CrO_3–pyridine complex (10 eq) in CH_2Cl_2 (25 ml) under stirring. The mixture was stirred at room temperature for 17 h. The mixture was poured onto ice and filtered through a Celite layer. The Celite layer was washed with Et_2O. The filtrate and washings were combined and extracted with Et_2O. The Et_2O layer was washed with dilute HCl, saturated $NaHCO_3$ and saturated NaCl, and dried over $MgSO_4$. The solvent was evaporated off under vacuum, and the residue was separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 4:1) to give **1** (64 mg, 33%) and a mixture of 4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**3**) and 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**4**) (1:2, ^{19}F-NMR peak ratio, 33.5 mg, 16%). The mixture of **3** and **4** was separated by medium pressure liquid chromatography (Kusano Kagaku: CPS-HS-221, hexane–2-propanol, 30:1). **3**: Colorless needles. mp 89—91 °C. MS *m/z*: 208 (M^+). HRMS Calcd for $C_9H_{11}F_3O_2$: 208.071. Found: 208.071. ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, s), 1.52—2.74 (4H, m), 2.74—3.08 (1H, m), 3.24 (1H, s), 6.15 (1H, ddd, J = 10.3, 2.9, 0.7 Hz), 7.18 (1H, ddd, J = 10.3, 2.1, 2.1 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 16.44 (s). **4**: Colorless oil. MS *m/z*: 208 (M^+). HRMS Calcd for $C_9H_{11}F_3O_2$: 208.071. Found: 208.071. ^{1}H-NMR ($CDCl_3$) δ: 1.60 (3H, s), 1.90—2.20 (2H, m), 2.32—2.58 (4H, m), 2.97 (1H, s), 6.32 (1H, s). ^{19}F-NMR ($CDCl_3$) ppm: 16.61 (s).

Oxidation of 1 with CrO_3–3,5-Dimethylpyrazole (DMP) Complex A solution of **1** (194 mg, 1 mmol) in CH_2Cl_2 (1 ml) was added to a suspension of CrO_3–DMP complex (10 eq) in CH_2Cl_2 (15 ml) at −20 °C and stirred at this temperature for 1 h. After work-up as above, the residue was purified on an SiO_2 column in CH_2Cl_2 solution to give a mixture of **3** and **4** (1:4, ^{19}F-NMR peak ratio, 107 mg, 51%).

Oxidation of 1 with CrO_3 in AcOH A solution of **1** (194 mg, 1 mmol) and CrO_3 (0.3 g, 3 mmol) in AcOH–H_2O (3:1, 2 ml) was stirred at room temperature for 15 h. After usual work-up, the residue (95 mg) was analyzed by GLC (15% SE-30, 1 m × 4 mm, 100 °C, N_2, 30 ml/min); it contained **1** (32%, peak area) and a mixture of **3** and **4** (51%).

Oxidation of 1 with *tert*-BuOOH Catalyzed by CrO_3 A solution of **1** (388 mg, 2 mmol) in CH_2Cl_2 (2 ml) was added to a solution of 70% *tert*-BuOOH (2.8 ml, 20 mmol) and CrO_3 (10 mg, 0.1 mmol) in CH_2Cl_2 (8 ml), and the mixture was stirred at room temperature for 14 h. The reaction mixture was passed through an Al_2O_3 column and the column was washed with Et_2O. The organic layer and washing were combined and concentrated under vacuum. The residue was purified by column chromatography (SiO_2, CH_2Cl_2) to give a mixture of **3** and **4** as a colorless oil (2:1 from ^{19}F-NMR peak ratio, total 277 mg, 67%).

Oxidation of 1 with *tert*-BuOOH Catalyzed by $Cr(CO)_6$ A solution of $Cr(CO)_6$ (110 mg, 0.5 mmol), 70% *tert*-BuOOH (0.2 ml, 1.5 mmol) and **1** (194 mg, 1 mmol) in CH_3CN (5 ml) was stirred for 14 h under reflux. The mixture was passed through an Al_2O_3 column and the column was washed with Et_2O. The organic layer and washing were concentrated under vacuum and the residue was purified by column chromatography (SiO_2, CH_2Cl_2) to give a mixture of **3** and **4** (2:1 from GLC, 114 mg, 55%).

1-Methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-ol (9,9,9-Trifluoro-*p*-menth-2-ene-1,8-diol, 5) A solution of 1-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-2-cyclohexen-1-one (**3**, 163 mg, 0.78 mmol) in Et_2O (2 ml) was added to a solution of MeMgI (3 mmol) in Et_2O (3 ml) and the mixture was stirred for 4 h. The reaction mixture was poured into ice-diluted HCl and extracted with Et_2O. The Et_2O layer was washed with saturated $NaHCO_3$ and saturated NaCl, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO_2, CH_2Cl_2–Et_2O, 10:1) to give **5** (97 mg, 56%). This was found to be a mixture of two diastereomers (**5a** and **5b**, ratio 2:5 based on the peak ratio on ^{19}F-NMR), which were separated by rechromatography. **5a** (the first eluate): Colorless needles. mp 97—100 °C. MS *m/z*: 224 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O_2$: 224.102. Found: 224.103. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (6H, s), 1.50—1.65 (3H, m), 1.75—1.82 (1H, m), 1.84—1.91 (1H, m), 2.16 (1H, br s), 2.45—2.52 (1H, m), 5.85 (1H, ddd, J = 10.4, 2.0, 2.0 Hz), 5.90 (1H, d, J = 10.4 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 16.34 (s). **5b** (the second eluate): Colorless needles. mp 143—144 °C. MS *m/z*: 224 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O_2$: 224.102. Found: 224.103. ^{1}H-NMR (CD_3COCD_3) δ: 1.27 (3H, d, J = 0.9 Hz), 1.30 (3H, s), 1.40—1.72 (3H, m), 1.87—1.98 (2H, m), 2.03 (1H, br s), 2.54—2.64 (1H, m), 5.77 (1H, d, J = 10.5 Hz), 5.82 (1H, ddd, J = 10.5, 2.4, 1.5 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 15.96 (s). The structure of **5b** was established by X-ray analysis, and has a *cis* relation between the 1-CH_3 group and the 4-(2,2,2-trifluoro-2-hydroxy-1-methylethyl) group.

4-(2,2,2-Trifluoro-1-hydroxy-1-methylethyl)cyclohexanone (6) A solution of **3** (416 mg, 2 mmol) in MeOH (5 ml) was shaken in a stream of hydrogen with 5% Pd–C (25 mg) at room temperature. After absorption of 43 ml of hydrogen, the catalyst was filtered off. The filtrate was evaporated under vacuum to give **6** (532 mg, unpurified, quantitative). **6**: Colorless viscous oil. MS *m/z*: 210 (M^+). HRMS Calcd for $C_9H_{13}F_3O_2$: 210.087. Found: 210.086. ^{1}H-NMR ($CDCl_3$) δ: 1.22—1.91 (2H, m), 1.37 (3H, s), 2.00—2.63 (7H, m), 3.71 (1H, br s). ^{19}F-NMR ($CDCl_3$) ppm: 16.13 (s).

1-Methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexanol (7) A solution of **6** (337 mg, 1.6 mmol) in Et_2O (3 ml) was added dropwise to a solution of MeMgI/Et_2O (10 mmol) and the mixture was refluxed for 4.5 h. After a usual work-up, the residue was purified by column chromatography (SiO_2, CH_2Cl_2–Et_2O, 3:1) to give **7** (341 mg, 94%). Analysis of **7** by GLC (3% OV-1, 1 m × 4 mm 100 °C, N_2, 30 ml/min) showed that it contained two diastereomers (2:3), which were separated by rechromatography. **7**: One isomer (the first eluate): Colorless needles. mp 89—91 °C. MS *m/z*: 226 (M^+). HRMS Calcd for $C_{10}H_{17}F_3O_2$: 226.118. Found: 226.118. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, s), 1.31 (3H, s), 1.34—1.80 (10H, m), 2.50 (1H, s). ^{19}F-NMR ($CDCl_3$) ppm: 15.86 (s). The other isomer: Colorless needles. mp 106—111 °C. MS *m/z*: 226 (M^+). HRMS Calcd for $C_{10}H_{17}F_3O_2$: 226.118. Found: 226.119. ^{1}H-NMR ($CDCl_3$) δ: 1.12—1.38 (2H, m), 1.25 (3H, s), 1.30 (3H, s), 1.41—1.52 (2H, m), 1.52—1.87 (5H, m), 1.87—1.95 (1H, m), 2.29 (1H, s). ^{19}F-NMR ($CDCl_3$) ppm: 15.90 (s).

1-Methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (Trifluoro-α-terpineol, 8) A solution of **7** (240 mg, 1 mmol) and $POCl_3$ (183 mg, 1.2 mmol) in pyridine (1 ml) was stirred at room temperature for 16 h. After a usual work-up, the residue was purified by column chroma-

tography (SiO_2, hexane–CH_2Cl_2, 1 : 1) to give **8** (147 mg, 67%). **8**: Colorless oil. bp 90 °C/15 mmHg (bulb to bulb distillation). MS *m/z*: 208 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O$: 208.107. Found: 208.107. ^{1}H-NMR ($CDCl_3$) δ: 1.20—1.40 (3H, m), 1.66 (3H, s), 1.78—2.41 (8H, m), 5.27—5.49 (1H, m). ^{19}F-NMR ($CDCl_3$) ppm: 15.96 (s), 16.42 (s) (peak ratio 1 : 1).

1-Methyl-4-(1,1,1-trifluoro-2-tosyloxy-2-propyl)cyclohexene (9) A solution of **8** (104 mg, 0.5 mmol) in tetrahydrofuran (THF) (2 ml) was added to a suspension of 60% NaH (30 mg, 0.75 mmol) in THF (1 ml) at 0 °C. The mixture was stirred at room temperature for 10 min, then a solution of *p*-TsCl (143 mg, 0.75 mmol) in THF (2 ml) was added at 0 °C to the mixture. The mixture was stirred at room temperature for 9.5 h and worked up as usual. The residue was purified by column chromatography (SiO_2, pentane–CH_2Cl_2, 4 : 1) to give **9** (108 mg, 60%). **9**: Colorless viscous oil. MS *m/z*: 207 (M − Ts), 190 (M − TsOH). HRMS Calcd for $C_{10}H_{14}F_3O$ (M − Ts): 207.100. Found: 207.100. ^{1}H-NMR ($CDCl_3$) δ: 1.05—2.40 (10H, m), 1.64 (3H, s), 2.44 (3H, s), 5.24—5.44 (1H, m), 7.32 (2H, d, J=8.0 Hz), 7.80 (2H, d, J=8.0 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 12.92 (s), 13.35 (s) (peak ratio 1 : 1).

1-Methyl-4-[1-(trifluoromethyl)ethenyl]cyclohexene (Trifluorolimonene, 10) and 1-Methyl-4-[methyl(trifluoromethyl)methylene]cyclohexene (11) A solution of **9** (372 mg, 1 mmol) and *tert*-BuOK (179 mg, 1.6 mmol) in THF (2 ml) was stirred at room temperature for 3 h. A usual work-up gave a colorless oil (208 mg). Analysis of this oil with ^{19}F-NMR spectroscopy and GLC (15% SE-30 1 m × 4 mm, 50 °C, N_2, 30 ml/min) showed that it was a mixture of **10**, **11** and **8** (73 : 3 : 7 from GLC peak area; yields were calculated to be 78%, 4% and 7%, respectively). Separation by preparative GLC (15% SE-30 1 m × 4 mm, 50 °C, He, 30 ml/min) give a mixture of **10** and **11**. (The amount of **11** was too small to be observed on ^{1}H-NMR.) **10**: Colorless oil. MS *m/z*: 190 (M^+). HRMS Calcd for $C_{10}H_{13}F_3$: 190.097. Found: 190.097. ^{1}H-NMR ($CDCl_3$) δ: 1.15—2.60 (7H, m), 1.66 (3H, s), 5.28—5.48 (2H, m), 5.70 (1H, q, J=1.5 Hz). ^{19}F-NMR ($CDCl_3$) ppm: 4.55 (s). Another small peak was observed at 4.73 ppm (s). This seemed to be due to **11**. The GLC-MS result was consistent with the expected structure. MS *m/z*: 190 (M^+). HRMS Calcd for $C_{10}H_{13}F_3$: 190.097. Found: 190.096.

3-(2,2,2-Trifluoro-1-hydroxy-1-methylethyl)cyclohexanone (12) A solution of **4** (178 mg, 0.86 mmol) in MeOH (5 ml) was shaken with 5% Pd–C (10 mg) in a stream of hydrogen at room temperature. After absorption of hydrogen had ceased, the mixture was worked up as in the case of **6** to give **12** as a colorless viscous oil (180 mg, unpurified, quantitative). **12**: MS *m/z*: 210 (M^+). HRMS Calcd for $C_9H_{13}F_3O_2$: 210.087. Found: 210.086. ^{1}H-NMR ($CDCl_3$) δ: 0.77—2.74 (9H, m), 1.36 (3H, s), 2.91 (1H, br s). ^{19}F-NMR ($CDCl_3$) ppm: 15.64 (s), 15.80 (s) (peak ratio 1 : 1).

1-Methyl-3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexanol (13) A solution of **12** (253 mg) in Et_2O (3 ml) was added to a solution of MeMgI/Et_2O (3 mmol), and the mixture was stirred at room temperature for 36 h. After a usual work-up, the residue was separated by column chromatography (SiO_2, CH_2Cl_2–Et_2O, 10 : 1) to give **13** (175 mg, 64%, overall yield from **4**) and **12** (92 mg, 36%). **13**: Colorless viscous oil. MS *m/z*: 226 (M^+), 211 (M − CH_3), 208 (M − H_2O). HRMS Calcd for $C_{10}H_{15}F_3O$ (M − H_2O): 208.108. Found: 208.108. ^{1}H-NMR ($CDCl_3$) δ: 0.67—2.41 (15H, m), 2.86 (2H, s). ^{19}F-NMR ($CDCl_3$) ppm: 14.96 (s), 15.48 (s), 15.66 (s), 15.76 (s) (peak ratio 4 : 4 : 1 : 2).

2-Methyl-4-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (14) and 1-Methyl-3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)cyclohexene (15) A mixture of **13** (327 mg, 1.45 mmol), $POCl_3$ (230 mg, 1.5 mmol) and pyridine (2 ml) was stirred at room temperature for 15 h. After a usual work-up, the residue was separated by column chromatography (SiO_2, hexane–CH_2Cl_2, 1 : 1) to give a mixture of dehydration products (237 mg, 79%). Analysis of this mixture by GLC (90 °C) and HPLC (POLYGOSIL 4.6 mm × 150 mm, hexane–2-propanol, 250 : 1, RI-detector) showed that it contained four isomers. This was separated by preparative GLC (15% DEGS 2 m × 4 mm, 100 °C, He, 30 ml/min). The spectral data for these products are as follows (in the order of retention time; ratio 9 : 16 : 10 : 65).

i) Colorless oil. MS *m/z*: 208 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O$: 208.107. Found: 208.108. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, q, J=0.9 Hz), 1.27—1.35 (1H, m), 1.44—1.57 (1H, m), 1.71 (3H, s), 1.74—2.04 (5H, m), 2.51—2.60 (1H, m), 5.48 (1H, br s). ^{19}F-NMR ($CDCl_3$) ppm: 16.14 (s).

ii) Colorless oil. MS *m/z*: 208 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O$: 208.107. Found: 208.108. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (3H, q, J=0.9 Hz), 1.32—1.42 (1H, m), 1.46—1.57 (1H, m), 1.69 (3H, s), 1.82—2.01 (5H, m), 2.52—2.62 (1H, m), 5.38 (1H, br s). ^{19}F-NMR ($CDCl_3$) ppm: 15.82 (s).

iii) Colorless oil. MS *m/z*: 208 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O$: 208.107. Found: 208.108. ^{1}H-NMR ($CDCl_3$) δ: 1.16—1.37 (2H, m), 1.32 (3H, q, J=1.2 Hz), 1.70—2.03 (6H, m), 2.27—2.35 (1H, m), 2.41—2.47 (1H, m), 4.65—4.69 (2H, m). ^{19}F-NMR ($CDCl_3$) ppm: 15.79 (s).

iv) Colorless oil. MS *m/z*: 208 (M^+). HRMS Calcd for $C_{10}H_{15}F_3O$: 208.107. Found: 208.108. ^{1}H-NMR ($CDCl_3$) δ: 1.17—1.30 (1H, m), 1.31 (3H, q, J=1.2 Hz), 1.66 (3H, br s), 1.80—2.17 (7H, m), 5.41 (1H, br s). Another peak attributed to a methyl group of a diastereomer was observed at 1.34 (q, J=1.2 Hz). ^{19}F-NMR ($CDCl_3$): 16.30 (s), 15.99 (s) (peak ratio 4 : 1). [Based on the chemical shift of the methyne hydrogen at C-3, iv was assigned to **14**, i and ii to **15** and iii to 3-(2,2,2-trifluoro-1-hydroxy-1-methylethyl)-1-methylenecyclohexane (**16**). The ratio on GLC showed that **14** : **15** : **16** was 65 : 25 : 10.

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References and Notes

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